

Surgical, Pharmacological, and Technological Advances in Adult and Pediatric Urology—State of the Art

*Highlights of the 8th Annual NYU Department of Urology Post-Graduate Course
December 6-8, 2001, New York, NY*

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The Department of Urology of New York University (NYU) School of Medicine hosted its 7th Annual Post-Graduate Course, December 6–8, 2001, entitled “The Surgical, Pharmacological and Technological Advances in Adult and Pediatric Urology—State of the Art.” The course was attended by urologists representing 32 states and 12 countries. The program focused on controversies in urologic oncology, pediatric urology, voiding dysfunction and incontinence, erectile dysfunction,

and infertility. It is not feasible to present in a single meeting summary all the clinically important information presented at this 2½-day meeting. Therefore, this review will highlight the information felt to be of greatest interest to the practicing urologist.

Controversies in Urologic Oncology

The session entitled “Controversies in Urologic Oncology” was moderated by Dr. Samir S. Taneja, Assistant Professor of Urology and Director of Urologic Oncology at NYU School of Medicine. Dr. Taneja described several cases that illustrated controversial management issues in urologic

oncology, and then contrasting management strategies were presented.

Positive Surgical Margins Following Radical Prostatectomy

The first case Dr. Taneja presented was that of a 52-year-old male with a Gleason 6 score and stage T1c prostate cancer, who was found to have a positive surgical margin at the time of radical prostatectomy. Dr. Taneja first argued for observation. He pointed out that although the prognosis for individuals with a positive margin is worse than that for those without a positive margin, most fail because of metastatic disease. Dr. Taneja argued that those

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with "bad" disease, defined by high-grade or seminal vesical invasion, are highly likely to have metastatic disease if they have extracapsular extension. For this reason, they are unlikely to benefit from immediate adjuvant irradiation. Those with a Gleason score ≤ 7 are most likely to benefit from adjuvant irradiation, and the majority will not relapse. Dr. Taneja felt that the best course was to observe these individuals and offer radiation only at the time of biochemical relapse, thereby potentially avoiding the inevitable toxicity of radiation. He presented data on a large, prospective study currently taking place at NYU, in which individuals with biochemical relapse following radical prostatectomy are being observed for 6 months. Those who maintain a low prostate-specific antigen (PSA) velocity over 6 months are offered empiric irradiation. To date, 29 patients have undergone irradiation by this protocol, with a 55% complete response at a mean follow-up of 18 months. PSA velocity strongly correlates with the likelihood of a response to radiation.

Dr. William Bedford Waters, Professor of Urology at the University of Tennessee Medical Center in Knoxville argued for immediate adjuvant irradiation. Dr. Waters agreed that the majority of individuals with high-grade disease or extracapsular extension would not benefit from radiation. He did, however, feel that immediate adjuvant radiation for a positive margin would benefit those with well-differentiated or moderately differentiated disease. He presented data from several series demonstrating prolonged disease-free survival among those undergoing immediate irradiation. Although he did not advocate radiation for all patients with a positive surgical margin, he did suggest that consideration should be given to radiation for select patients.

Intrarenal 3-cm Renal Mass

Another case presented by Dr. Taneja was that of a 45-year-old female with an incidental 2.8-cm renal mass that was largely intrarenal in location. Dr. Taneja argued in favor of open partial nephrectomy, whereas Dr. Michael Stifelman, Director of Laparoscopic Surgery in the Department of Urology at NYU School of Medicine, discussed the option of laparoscopic nephrectomy. Dr. Taneja pointed out that laparoscopic partial nephrectomy techniques likely would not be utilized by most surgeons in cases of larger intrarenal lesions. He raised the issue that in the contemporary era, a growing concern might be that individuals with small renal lesions, normally amenable to a partial nephrectomy, might be considered for laparoscopic nephrectomy in order to avoid an open incision. He noted that outcomes with partial nephrectomy are equivalent to those with radical nephrectomy for smaller tumors, and that in contemporary series, tumor size is not necessarily a contraindication to partial nephrectomy for properly located lesions. Dr. Taneja gave several reasons for considering partial nephrectomy, including 1) longer life-expectancy of patients in general; 2) a higher likelihood of contralateral metachronous lesions, given the prolonged longevity; 3) a demonstrated increase in the likelihood of renal insufficiency in long-term follow-ups of radical nephrectomy patients; and 4) a decreased likelihood of surgical morbidity owing to improved preoperative imaging with a three-dimensional reconstruction of computed tomography (CT) and/or magnetic resonance imaging (MRI).

Dr. Stifelman made the argument that although partial nephrectomy might be feasible in the hands of a skilled, experienced operator, it offered no advantage over radical nephrec-

tomy for this patient. He presented long-term follow-up data of patients undergoing radical nephrectomy, demonstrating no increased risk of renal failure or need for dialysis. Given the absence of an obvious advantage to partial nephrectomy, he then outlined what he felt to be a multitude of advantages to the laparoscopic approach, including a shorter hospital stay, a decreased need for postoperative pain medication, and a shorter recuperation with a quicker return to work in most cases. Dr. Stifelman countered Dr. Taneja's concern regarding multifocality by stating that the 12%–13% risk of multifocality noted in most series was all the more reason to consider a laparoscopic nephrectomy, in order to reduce the risk of ipsilateral recurrence. Although he did not discuss delayed cancer relapse, he did point out that, to date, no laparoscopic series has reported an increased risk of recurrence compared to open techniques.

High-Grade Prostatic Intraepithelial Neoplasia

Dr. Taneja spoke about the approach to high-grade prostatic intraepithelial neoplasia (HGPIN). He stated that although HGPIN generally has been classified as premalignant, no long-term data exists regarding the natural history of the lesion. Although a strong association between HGPIN and prostate cancer exists, there is no clear data regarding what percentage of patients with HGPIN will eventually develop prostate cancer. Dr. Taneja felt that in managing the patient with HGPIN, two issues were paramount: 1) ruling out occult coexisting cancer at baseline, and 2) ruling out the development of cancer at a later date. He presented two NYU studies designed to assess these questions. In the first, patients with HGPIN noted on a 12-core sampling of the prostate

received a repeat 12-core biopsy within a year of diagnosis. Only 2.4% of the patients were noted to have cancer on the repeat biopsy, suggesting that 12 cores at the time of diagnosis are adequate to rule out concomitant cancer in the absence

multicenter, randomized trial of neoadjuvant chemotherapy to cystectomy alone. In this study, conducted by the Southwest Oncology Group, a survival advantage was noted for those individuals undergoing neoadjuvant chemotherapy. Dr. Waters

Only 2.4% of the patients were noted to have cancer on the repeat biopsy, suggesting that 12 cores at the time of diagnosis are adequate to rule out concomitant cancer in the absence of other high-risk features (atypia, markedly increased PSA).

of other high-risk features (atypia, markedly increased PSA). In the second study, patients diagnosed with HGPN on a 12-core biopsy were subjected to a delayed-interval biopsy 3 years after the diagnosis. Of these men, 25.8% were found to have cancer regardless of the interval change in PSA. Dr. Taneja concluded that PSA is not an adequate means of following patients with HGPN and that delayed-interval biopsy 3 years after diagnosis is mandatory in all patients.

Neoadjuvant and Adjuvant Chemotherapy for Invasive Bladder Cancer

In the final lecture, Dr. Waters discussed the role of neoadjuvant or adjuvant chemotherapy in patients undergoing radical cystectomy for locally advanced bladder cancer. He reviewed the contemporary literature extensively and pointed out that although several randomized trials of adjuvant chemotherapy following cystectomy have been undertaken, none have been completed, either owing to early termination or protocol violation. He noted that the results reported to date have strongly favored the use of adjuvant chemotherapy in individuals with regional lymph node involvement or perivesical fat invasion. Dr. Waters reviewed the results of a large, recently reported,

pointed out that this study was strongly criticized because it used one-tailed statistics, which increases the likelihood of obtaining statistically significant findings. He noted that other studies conducted to assess the value of neoadjuvant chemotherapy in patients with locally advanced bladder cancer have failed to demonstrate a survival advantage.

Pediatric Urology

The session entitled "Prenatal Hydronephrosis" was moderated by Dr. Ellen Shapiro, Professor of Urology and Director of Pediatric Urology at NYU School of Medicine.

7 mm is the upper limit of the normal anterior-posterior diameter of the fetal renal pelvis.

The faculty included Drs. Michael Ritchey, Professor and Chairman of the Department of Urology, University of Texas Medical School, Houston, and Richard Rink, Professor of Urology and Chief of Pediatric Urology at the James Whitcomb Riley Hospital for Children at Indiana University School of Medicine.

Prenatal Hydronephrosis

Dr. Ritchey presented an update on the

management of prenatal hydronephrosis. He began his presentation with a review of the data from Sairam and associates on the implications of fetal pelvic measurement. The authors recently reported that 7 mm is the upper limit of the normal anterior-posterior diameter of the fetal renal pelvis. They noted that fetuses with an average renal pelvis diameter of < 7 mm had an excellent prognosis without surgical intervention. Attempts have also been made to compare renal dilation with gestational age and to correlate these findings with postnatal outcomes. Siemens and colleagues reported that anterior-posterior renal pelvic diameters < 6, < 8, and < 10 mm at < 20, 20–30, and > 30 weeks gestation, respectively, were not associated with significant clinical sequelae. Most cases of significant obstructive uropathy, such as those associated with posterior urethral valves, may be detected as early as the second trimester, but most cases of hydronephrosis and reflux become evident in the third trimester.

Dr. Ritchey reviewed the report of Holmes and associates that addresses antenatal intervention for severe

obstructive bilateral uropathy. This retrospective study, which reviewed the University of California, San Francisco, fetal surgery database from 1981 to 1999, evaluated the results of 36 fetuses that underwent antenatal surgery. The authors reported the long-term follow up of 14 of the 36 patients whose obstruction was caused by posterior urethral valves. Only 8 of the 14 survived, and 5 of these 8 surviving neonates developed chronic renal failure.

Therefore, it is assumed that despite favorable urinary electrolytes and the absence of dysplasia on sonogram, antenatal intervention will most likely not improve or prevent renal failure.

Dr. Ritchey reviewed the postnatal evaluation of neonates with antenatal hydronephrosis, indicating that most experts recommend a postnatal ultrasound and voiding cystourethrogram. It has been shown that even with an initial normal postnatal ultrasound, 25% will have reflux. According to Dr. Ritchey, all infants should be placed on amoxicillin prophylaxis until it has been shown that there is no reflux or dilation of clinical significance. One of the more interesting areas related to prenatal hydronephrosis is the incidence of severe vesicoureteral reflux, which is 3 to 5 times higher in males than in females. Sillen showed that these infants had an increase in the thickness of the bladder wall, and the study's urodynamic evaluations demonstrated higher voiding pressures, decreased bladder capacity, and hypercontractility. Farhat and colleagues found that the kidneys associated with high grades of reflux often show renal dysplasia, even in the absence of urinary tract infection. Godley and associates reviewed the natural history of vesicoureteral reflux in infants. Those infants with normal kidneys had a 100% resolution of the reflux. However, when there were bilateral abnormalities in the kidneys, only 10% spontaneously resolved their reflux. Most of the infants who failed to resolve the reflux had grade III vesicoureteral reflux. Infants with prenatal hydronephrosis caused by high-grade reflux had a greater overall resolution rate of their reflux than older children had.

Dr. Ritchey discussed the management of various case scenarios of postnatal ultrasound. One important caveat mentioned is that all infants

with persistent hydronephrosis require periodic radiographic follow-up. It has been shown that some infants with an initial nonobstructed pattern on a radioisotope diuretic renogram may later convert to an obstructed pattern.

Vesicoureteral Reflux

Dr. Ellen Shapiro presented an update on the management of vesicoureteral reflux. Dr. Shapiro cited a recent report by Herndon and colleagues that provides compelling evidence that pelvic floor muscle dysfunction has a fundamental role in the pathogenesis of reflux. The authors proposed aggressive treatment of voiding dysfunction and constipation as an important step in the diminution of

success, its clinical utility has been limited by its lack of durability. Although Deflux decreases in volume after implantation, animal studies have demonstrated an ingrowth of collagen between the microspheres that stabilizes the volume. This study enrolled 72 boys and 149 girls between the ages of 1 and 15 years with primarily grade III or IV vesicoureteral reflux, who received up to two more implantations after treatment. Of 221 children in the efficacy population, 67 received two implantations, whereas 8 received three implantations.

A voiding cystourethrogram (VCUG) was performed at 3 and 12 months postoperatively. The Deflux injec-

One of the more interesting areas related to prenatal hydronephrosis is the incidence of severe vesicoureteral reflux, which is 3 to 5 times higher in males than in females.

recurrent tract infections and the ultimate resolution of reflux. They recommended that children undergo pelvic floor muscle retraining; anticholinergics were not used initially in any of the patients. The mean follow-up was 2 years. Of 49 girls and 4 boys, aged 4–13 years, representing 72 refluxing renal units and varying grades of reflux, reimplantation surgery was performed in only 1 patient (2%). Further, during a 2-year period, one of the authors noted a > 90% decrease in reflux surgery.

The timing of this postgraduate course coincided with the recent U.S. Food and Drug Administration's (FDA) approval of Deflux, or dextranomer/hyaluronic acid copolymer. Lackgren and associates recently reported long-term efficacy and safety using this product for the endoscopic treatment of vesicoureteral reflux. To date, although bovine collagen has been shown to have good initial

tions were carried out using a 10-Fr cystoscope and a 3.5-Fr needle. The clinical follow-up period was 2 to 7.5 years, with a mean of 5 years. At the last VCUG, 81% had no dilating reflux, defined as less than grade III. A late VCUG was also performed on 49 patients, 2–5 years postoperatively. The study showed that if there was no reflux at 3 and 12 months, 96% of the patients remained free of dilating reflux. The study also found that the response rate was associated with the grade of reflux: grade III and grade IV reflux had a 73% and 59% response rate, respectively. There was essentially no morbidity associated with the procedure; only 8% of patients developed urinary tract infections, and almost all were girls. The development of pyelonephritis in this group was associated with voiding dysfunction.

Common Pediatric Urology Problems
The final presentation in the pediatric

session was given by Dr. Richard C. Rink. Dr. Rink reviewed a number of common pediatric urological problems. He examined the findings and treatment of the buried penis, hypospadias, the acute scrotum, and abnormal scrotal findings, including varicoceles. He also discussed the

vagina has the capacity to retain up to a liter of mucus; therefore, a palpable suprapubic mass may be present. A simple incision or hymenotomy permits satisfactory drainage.

In 10% of girls with ureterocele, the ureterocele may prolapse and present as a cystic mass originally from the

Boone, Professor and Chairman of the Department of Urology at Baylor School of Medicine, and Michael B. Chancellor, Professor of Urology at the University of Pittsburgh.

LUTS in Women

Dr. Nitti opened the session with a discussion on lower urinary tract symptoms (LUTS) in women. LUTS are common in women; they are often synonymous with an overactive bladder. There are many causes of LUTS, including detrusor overactivity, sensory urgency, impaired detrusor contractility, and functional and anatomical bladder-outlet obstruction. It was emphasized that in those women undergoing urodynamic testing for the evaluation of LUTS, complete testing that includes an evaluation of the voiding phase should be performed. Previous work from NYU has shown that 33% of women being evaluated for LUTS with urodynamics have abnormalities of the voiding phase. These abnormalities include dysfunctional voiding, primary bladder-neck obstruction, an anatomical obstruction from impaired

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approach to the nonpalpable testis and the role of laparoscopy for diagnosis, as well as the use of laparoscopy to perform a single or first-stage Fowler-Stephens procedure or standard orchidopexy.

Dr. Rink reviewed the differential diagnosis of interlabial masses in the female, including paraurethral cyst, urethral prolapse, imperforate hymen, ectopic ureterocele, and sarcoma botryoides. Paraurethral gland cysts result from retained secretions in the Skene's gland secondary to ductal obstruction and may displace the urethra to one side. Most of the cysts drain spontaneously or regress within 4–8 weeks. In some cases, the cyst may need to be incised. Urethral prolapse is usually seen in black females, 3–9 years of age, and presents with blood spotting on their underclothing. A physical examination will reveal a purplish red circumferential mass. Estrogen cream as well as steroid creams have been utilized, and sitz baths are begun if there is no improvement. Formal excision of the prolapsed tissue, which is the version of urethral mucosa, is recommended. An imperforate hymen presents as a bulging interlabial mass most commonly in the newborn; it is caused by retained vaginal secretions secondary to stimulation by maternal estrogens. The infant or older patient may present with hydrocolpos. The

urethra. It is usually erythematous or ischemic purplish or black in appearance. An ultrasound will usually confirm upper-tract hydroureteronephrosis. The ureterocele needs to be reduced manually, and a catheter is then put in place for bladder drainage.

Finally, sarcoma botryoides (rhabdomyosarcoma) is an unusual cause of an interlabial mass. It appears as a grape-like cluster; there is usually associated hematuria or the passage of tissue fragments from the vagina. A vaginal mass may be found on a bimanual examination. A sonogram of the pelvis and abdomen should be per-

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formed and followed by a CT scan. The biopsy is then performed; the most common histologic type is embryonal.

Voiding Dysfunction and Incontinence

The session on "Voiding Dysfunction and Incontinence" was moderated by Dr. Victor W. Nitti, Associate Professor and Vice-Chairman of the Department of Urology at NYU School of Medicine. Also on the faculty were Drs. Christopher Kelly and C.G. Xiao, Assistant Professors of Urology at NYU School of Medicine, Timothy B.

contractility, and an anatomical obstruction caused by cystoceles and prior incontinence surgery. Therefore, a urodynamic study can greatly affect treatment and outcome. The discussion also focused on LUTS in young women. In these cases, urodynamics seem to yield less unless the patient has a complaint of urge incontinence. In such cases, urodynamics can be the initial finding, suggesting a diagnosis of occult neurological disease, which can be confirmed when the patient is fully evaluated.

LUTS in Young Men

The discussion then focused on LUTS in young men. Dr. Nitti presented work done at NYU that showed that videourodynamics were the best single diagnostic test in this group of patients. Definitive diagnoses were made in 78% of young men (under 45 years of age) with LUTS. The most common diagnosis was primary vesicle-neck obstruction, which occurred in 47% of these men. Higher symptom scores (especially voiding or obstructive scores) and abnormal noninvasive uroflow rates help predict those men who will have urodynamic abnormalities.

Neurogenic Voiding Dysfunction

Dr. Boone then provided an overview of the manifestations of neurogenic voiding dysfunction, including abnormalities of filling, storage, and/or emptying. The most critical factor of all is bladder compliance. Individuals with high storage pressures secondary to poor compliance are at the greatest risk of developing renal insufficiency and other serious sequela. In general, impaired compliance is often the result of a functional outlet obstruction such as detrusor-internal sphincter dyssynergia or detrusor-external sphincter dyssynergia (DESD), which will also lead to impaired bladder emptying. Both of these occur in supra sacral spinal cord injuries or lesions. Lesions in the brain above the pontine micturition sector tend to give detrusor hyperreflexia without dyssynergia, and emptying and compliance issues are therefore much less common. Treatment of neurogenic voiding dysfunction must focus on assuring low storage pressures and facilitating emptying. Finally, symptoms such as incontinence, frequency, and urgency should be addressed via treatment modalities. Dr. Boone reviewed current therapies for neurogenic voiding dys-

function, including anticholinergic therapy and augmentation cystoplasty to improve compliance and reduce hyperreflexia; external sphincterotomy and urethral stenting to treat DESD; bladder-neck incision to treat detrusor-internal sphincter dyssynergia; and intermittent self-catheterization to treat emptying problems. Neuromodulation using both the Brindley stimulator (which is currently no longer available in the United States) and the Medtronic Interstim device may also have utility. Use of the Interstim device in patients with neurological disease must still be considered investigational, although some studies have reported success with this modality.

Future Management of Incontinence and Voiding Dysfunction

Dr. Chancellor discussed the future of the treatment of incontinence and voiding dysfunction into the next decade. Dr. Chancellor reviewed the idea of a new approach to treatment that focuses on prevention rather than on reactive therapy. He promoted the idea of afferent blockade, a revised approach to treatment that targets the afferent nerves to control the bladder, lower pressures, and improve incontinence. He stated that "Using anticholinergic agents for the treatment of an overactive bladder could be considered after-the-fact therapy. In essence it relies on waiting for the bladder to have a spasm and then tries to quiet it down. That is, it focuses on efferent bladder activity. It would be more desirable to prevent the micturition reflex that initiates the overactive bladder. There are a number of afferent blockade drugs now in development that can prevent the bladder from having an involuntary contraction."

Treating the patient with an overactive bladder from this approach

would provide the possibility of giving lower drug doses with fewer side effects as well as greater efficacy. Dr. Chancellor pointed out that drugs that act on the afferent nervous pathways do not present the risk of urinary retention that occurs with anticholinergic drugs. Approaches that could achieve this include advanced drug delivery systems, chili pepper extract therapy (capsaicin and resiniferotoxin), and gene therapy.

Advanced drug-delivery systems utilized for voiding dysfunction hold great potential. There are many advantages for these systems, including achievement of long-term therapeutic efficacy with decreased side effects and improved patient compliance. The downside currently is their high cost. Chili pepper extract therapy has received a great deal of attention and is favored by patients because of the ease of understanding this treatment option. This form of therapy is readily available as a topical capsaicin cream that can be obtained over the counter for the treatment of topical pain. Dr. Chancellor pointed out that the approach toward intravesical therapy that has received the most attention has been the instillation of pepper extracts in the bladder to act on the C-fiber vanilloid receptors.

Gene therapy is another source of hope for the treatment of an overactive bladder. Dr. Chancellor reports that gene therapy holds great promise for treating an overactive bladder because it is possible to access all the genitourinary organs via endoscopy and other minimally invasive techniques that are ideally suited for gene therapy. His studies on gene therapy show its potential value in the treatment of diabetic neurogenic bladder and interstitial cystitis. These studies have focused on the use of the herpes virus as a vector to deliver

therapy. Dr. Chancellor hopes that his continued studies on advanced drug-delivery systems and gene therapies will continue to produce highly promising results.

A Novel Approach to Managing a Neurogenic Bladder: The Skin-Central Nervous System-Bladder Reflex

The next discussion focused on a new National Institutes of Health

nence after radical prostatectomy. Most studies have shown that post-radical prostatectomy incontinence results from sphincteric insufficiency. Over 90% of patients with post-prostatectomy incontinence had sphincteric insufficiency, whereas isolated bladder dysfunction occurs in only a small percentage of patients. Sphincteric insufficiency often occurs because of injury of the rhab-

use of collagen should be reserved for patients in whom incontinence is not severe enough to warrant an artificial sphincter.

Finally, Dr. Nitti gave a presentation on the new male sling techniques. Short-term reports have shown success in 80% of patients, with about 45% becoming totally dry. The male sling techniques rely on external compression of the bulbar urethra from its underside, not circumferentially. Clearly, the advantage is that there are no mechanics involved. However, because it works on the same theory as early prostheses (for example, the Kaufman prosthesis), which proved to be less effective than the currently available artificial urinary sphincter, it is felt that sling procedures will probably not equal the artificial urinary sphincter in efficacy. They may, however, have a place in men with less severe incontinence and those desiring not to have a mechanical device.

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(NIH) protocol currently being conducted at the NYU School of Medicine, Department of Urology—the skin-central nervous system (CNS)-bladder reflex study being conducted by Drs. Xiao, Nitti, and Kelly. Drs. Kelly and Xiao reviewed Dr. Xiao's timely work in the early 1990s, when he created a new skin-CNS-bladder reflex pathway in rats. Using a spinal nerve crossover technique, the ventral root of an established somatic reflex arc, L4, was anastomosed to "the cut ventral" nerve root of L6 (autonomic nerves to the bladder) to create a new micturition reflex arc. Stimulation of the L4 dermatome produced a reflex bladder contraction in rats. This technique has been successfully applied to humans in China as presented by Dr. Xiao. Currently, NYU is the only medical center in the United States conducting an NIH-funded clinical trial examining the skin-CNS-bladder reflex in humans.

Post-Prostatectomy Incontinence

The final discussion on voiding dysfunction and incontinence was dedicated to post-prostatectomy incontinence. Dr. Nitti reviewed the etiology of post-prostatectomy incontinence, focusing mainly on inconti-

nosphincter during surgery; this can occur in the rhabdosphincter complex at the time of surgery in the form of direct injury to the sphincter, its nerve supply, or its supporting structures. Treatments for post-prostatectomy incontinence resulting from sphincteric insufficiency include biofeedback and pelvic floor muscle exercises, periurethral bulking agents such as collagen, artificial urinary sphincters, and the new male sling procedures. Dr. Nitti pointed out that biofeedback and pelvic floor muscle exercises seem to have their greatest effects early on and may not actually improve continence, but rather help patients to achieve their final level of continence quicker.

Dr. Boone then gave an extensive discussion on the artificial urinary sphincter. He focused on the current device, the American Medical Systems AMS-800 artificial urinary sphincter. This remains the "gold standard" for the treatment of post-prostatectomy incontinence; as many as 90% of patients have had satisfactory results from a large number of series. Dr. Boone also discussed the use of collagen, which in his practice has had much less effective results than an artificial sphincter. He felt that the

Erectile Dysfunction

The session entitled "Erectile Dysfunction" was moderated by Dr. Andrew R. McCullough, Assistant Professor and Director of Sexual Health and Fertility at the NYU School of Medicine. The faculty included Dr. Ridwan Shabsigh, Associate Professor of Urology at Columbia-Presbyterian Medical Center and Dr. Wayne Hellstrom, Professor of Urology at Tulane University.

The Socioeconomics of Erectile Dysfunction Practice

Dr. Shabsigh discussed the socioeconomics of erectile dysfunction (ED). Sildenafil citrate (Viagra) has changed the nature of the ED practice for urologists. Although fewer than 7% of men sought treatment before the advent of oral therapy, it is estimated that 20% of men at risk

have now been treated.

ED clearly has a detrimental impact on quality of life. Quality-of-life studies show that successful treatment of ED resulted in significant improvement in five out of eight

without pleasure, and absence of ejaculation. Over 30% of men across all ages experience premature ejaculation, and 4% retarded ejaculation. Serotonin is an important neurotransmitter in the control of ejacula-

to sildenafil, questionably fewer visual side effects, and lack of high-fat meal interaction. Tadalafil has a half-life that is 4 times that of sildenafil and no visual side effects, but it has a strong PDE-11 interaction. PDE-11 is found in the heart, pituitary, and testis; tadalafil's safety in the testis is under investigation. The safety implications of the long half-life need to be further scrutinized, although the side-effect profile of tadalafil is similar to that of sildenafil and vardenafil.

The high efficacy rates of sildenafil are also seen with the other PDE-5 inhibitors. Direct comparisons of their efficacy and side-effect profiles can be made only with direct comparator trials, because inclusion criteria and end point measurements differ between trials.

Sublingual apomorphine HCL. Apomorphine represents an innovation in oral therapy for ED. Unlike the PDE-5 inhibitors, which work peripherally, apomorphine works centrally. It is rapidly absorbed and has shown successful intercourse rates of 50% (vs 31% for placebo). The most disturbing side effect is syncope,

Urologists write approximately 18% of the sildenafil prescriptions, and primary care physicians account for 62% of the new prescriptions.

general quality-of-life parameters. With a successful treatment outcome in over 70% of patients, the treatment of ED will have a positive impact on the quality of life for many men and their partners. In the first 22 months after the approval of sildenafil there was a 428% increase in the number of patient visits for ED. Oral therapy currently accounts for 92% of the treatments for ED. Urologists write approximately 18% of the sildenafil prescriptions, and primary care physicians account for 62% of the new prescriptions. Unlike other prescription drugs such as atorvastatin calcium (Lipitor), where patients pay only 13% of the prescription costs, as many as 57% of sildenafil prescriptions are paid by patients.

It is highly probable that the introduction of at least 2 new oral therapies in the next 12 months will increase the demand for physician services for the treatment for ED. The increase in health care expenditures in this area will mandate closer scrutiny of outcome measures. The role of the urologist is evolving, and it will be important for urologists to maintain their leadership as educators and experts.

Understanding Ejaculatory Disorders

Dr. Hellstrom discussed ejaculatory disorders, which comprise the most common form of male sexual dysfunction. Ejaculatory dysfunctions can be unsatisfactory timing, ejaculation

tion at all levels. Increased serotonin levels result in decreased sexual activity, increased latency of ejaculation, increased seminal emission, decreased erectile function, and increased penile sensory threshold.

An Update on the Treatment of Erectile Dysfunction

Dr. Shabsigh presented an update on the treatment of ED. Sildenafil has revolutionized the treatment of ED. Despite initial concerns about the safety and efficacy of sildenafil treatment, post-launch experience has confirmed the safety and efficacy of the medication in all forms of ED, including ED with multiple comorbidities and risk factors. The only group

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in which sildenafil is contraindicated is men on organic nitrates.

Three oral medications and a topical treatment are currently under FDA review or soon to be reviewed.

Tadalafil and vardenafil. Both medications are phosphodiesterase type 5 (PDE-5) inhibitors with mechanisms of actions comparable to sildenafil. Vardenafil is the most sensitive PDE-5 inhibitor, with the lowest IC-50. It has a comparable half-life and time-to-peak serum concentration

which occurred in 0.6% of men in dose-optimization regimens with a median duration of 60 seconds. Syncope occurred with the first dose in 54% of men with an uneventful rechallenge in 53%. Other adverse events included nausea (15.0%), dizziness (9.4%), sweating (5.8%), somnolence (8.1%), and yawning (6.1%). Apomorphine has been approved and successfully launched in Europe in 2001 without major safety issues.

Topical prostaglandin E-1 gel. The

development of a topical absorption enhancer has allowed the development of a topical prostaglandin preparation. Initial trials published in *Urology* show a significant effect of the preparation over placebo in terms of the angle of erection. However,

improper control groups and short-term follow up have limited the objective evaluation and results.

Potaba (potassium aminobenzoate) was first reported in 1959 for the treatment of Peyronie's disease. This form of therapy has been reported to

because it delivers medication directly to the area of fibrosis. Several problems, however, are inherent in the injection process: It is sometimes difficult to palpate the plaque's location; there is uneven distribution of the injected medication because of the thickness and toughness of the plaque; and the process of injection itself may create more long-term fibrosis.

A study has shown that the use of intralesional steroids results in the improvement in symptoms in 36% of patients. Patients with small, discrete plaques benefit the most from this therapy. However, local steroid-induced tissue atrophy can result in more difficult reparative surgery.

In vitro studies with verapamil have demonstrated the dependence on calcium for the extracellular transport of collagen. Verapamil, a calcium channel blocker, increases collagenase activity. Single-blinded studies have demonstrated a therapeutic benefit in patients with noncalcified plaques and with angulations of less than 30°. No significant complications were encountered.

In vitro studies have demonstrated decreased collagen production and increased collagenase activity with interferons α -2b and γ in Peyronie's disease-derived human fibroblasts.

Unlike the PDE-5 inhibitors, which work peripherally, apomorphine works centrally.

translating the angle of erection to success rates in intercourse remains to be defined. The gel has been well-tolerated, exhibiting symptoms of mild-to-moderate penile burning after application; no significant changes in vital signs were noted. Topical therapy appears to be a second-line therapy that will be embraced by the primary care physician.

Medical Therapy for Peyronie's Disease

Dr. Hellstrom presented an update on Peyronie's disease. The study of therapies for Peyronie's disease is fraught with logistical problems. The manifestation of the disease varies tremendously from patient to patient; the degree of angulation is difficult to measure reliably; and not all studies evaluate the patients with intracorporal injections, often relying on patient descriptions or photographs to "quantitate" the degree of angulation. Furthermore, quantification of plaque size by ultrasound is difficult and unreliable; few studies have adequate controls; and long-term follow up is frequently lacking.

Oral therapy. Vitamin E remains the most popular form of medical therapy for Peyronie's disease, mostly because of its low cost and lack of side effects. The efficacy of the treatment has been reported to range between 13% to 70%. As with many of Peyronie's disease studies, however,

result in decreased plaque and angulation in 25% to 70% of patients. However, the inconsistent results, expense, and gastrointestinal side effects often lead to low compliance with this form of therapy.

Tamoxifen is a nonsteroidal anti-estrogen that facilitates the release of transforming growth factor-beta (TGF- β) from human fibroblasts in vitro, suggesting that it can inhibit an inflammatory response and decrease fibroblast production and/or angiogenesis. Response rates of 30% have been shown. The lack of information on its mechanism of action and side-effect profile has limited its use in the United States.

Colchicine is an anti-inflammatory agent that can decrease collagen synthesis and stimulate collagenase

The study of therapies for Peyronie's disease is fraught with logistical problems.

activity. It interferes with the transcellular movement of collagen and diminishes the activity of the enzymes responsible for collagen processing. In noncontrolled studies, a 37% decrease in curvature and a 50% decrease in plaque size have been reported. However, a reported 50% incidence of gastrointestinal upset limits its use.

Intralesional therapy is attractive

The limited success of intralesional verapamil and collagenase led to the use of interferon as an intralesional agent. Improvement in phallalgia, curvature, and "objective" decrease in plaque sizes have been reported in a small, single-blind, placebo-controlled study. Complications have included fever, a flu-like syndrome, and arthralgias. The side effects, however, are short-lived and respond

to nonsteroidal anti-inflammatory drugs. The lack of standardization of injection dose, frequency of injections, and number of total injections make it next to impossible to compare studies. Large multicenter, single-blind, placebo-controlled studies are ongoing.

Shock-wave lithotripsy. Studies in Europe on shock-wave lithotripsy have

shortening of the penis.

Penile grafting. Numerous autogenous and synthetic materials have been used for penile grafting. Favorable results have been reported with the use of both kinds of graft material.

Men with borderline preoperative function or arteriogenic disease should

In the era of in vitro fertilization/intracytoplasmic sperm injection, where sperm morphology and concentration cease to be an issue, many reproductive endocrinologists question the importance of varicocele repair.

shown minimal efficacy. Many experts fear that lithotripsy may induce aggravation of the underlying fibrosis.

Surgery. There is no one surgical procedure for the treatment of Peyronie's disease. Surgical alternatives include penile plication, grafting procedures, or penile implant surgery.

Penile plication. This is the least invasive of the surgical modalities and involves the least disturbance to the underlying corporal tissues. The results are generally favorable, but it is useful only for lesser degrees of deformity and invariably results in

seriously contemplate implant surgery as they may develop treatment-resistant ED. In men with co-existing ED or underlying penile vascular impairment as documented by penile duplex Doppler, the penile prosthesis remains the treatment of choice. Wilson has described molding the penis over the implant as a way of treating severe deformity. Alternatively, the combination of patching and implant can be used.

Infertility

The session entitled "Infertility" was

moderated by Dr. Andrew R. McCullough, Assistant Professor and Director of Sexual Health and Fertility at the NYU School of Medicine. The guest faculty included Dr. Arnold Belker, Clinical Professor at the University of Louisville, and Dr. Robert Rosen, Professor of Radiology at NYU School of Medicine.

Varicocele Surgery: Does it Make Sense in the Era of In Vitro Fertilization/Intracytoplasmic Sperm Injection?

Dr. Arnold Belker reviewed the data on the efficacy of varicocele on pregnancy rates. Although some studies fail to demonstrate any benefit to varicocele surgery, Madgar demonstrated the superiority of varicocele repair over nonintervention. In the era of in vitro fertilization/intracytoplasmic sperm injection (IVF/ICSI), where sperm morphology and concentration cease to be an issue, many reproductive endocrinologists question the importance of varicocele repair. In a study by Schlegel, however, the cost per delivered child after varicocele repair was \$26,268 versus \$89,091

Main Points

- In radical prostatectomy, the majority of patients with high-grade disease or extracapsular extension would not benefit from radiation. Immediate adjuvant radiation for a positive margin might benefit select patients with moderately differentiated disease.
- High-grade prostatic intraepithelial neoplasia generally has been classified as premalignant, but no long-term data exists regarding its natural history or how many patients eventually develop prostate cancer.
- Most prenatal cases of significant obstructive uropathy may be detected as early as the second trimester, but most hydronephrosis and reflux cases become evident in the third trimester. Antenatal intervention will most likely not improve or prevent renal failure.
- Current therapies for neurogenic voiding dysfunction include anticholinergics and augmentation cystoplasty; sphincterotomy, urethral stenting, and bladder-neck incision to treat sphincter dyssynergia; and intermittent self-catheterization to treat emptying problems. Another novel approach is via the skin-central nervous system-bladder reflex.
- The AMS-800 artificial urinary sphincter remains the "gold standard" for the treatment of post-prostatectomy incontinence. The new male sling procedures will probably not equal the artificial urinary sphincter in efficacy.
- Peyronie's disease is currently being managed orally with vitamin E, potassium aminobenzoate, tamoxifen, colchicine, intraleisional therapy, verapamil, and interferon. Other approaches being used are shock-wave lithotripsy, surgery, penile plication, and penile grafting.

after IVF/ICSI. Further, some studies have suggested that IVF efficiency is improved after varicocele repair. Finally, notwithstanding the improved

or misdiagnosed, and 15% were overdiagnosed by a physical examination. The improvement in seminal parameters in men with varicoceles

interventional radiologist cannot be underestimated.

In men presenting with infertility, there was a 38% incidence of clinical varicoceles; ultrasound diagnosed varicoceles in 76% of the men presenting.

pregnancy rates after varicocele repair, IVF alone, without the improvement of varicocele repair, incurs a potential health risk for the mother, including ovarian hyperstimulation syndrome and high multiple birth rates.

The Role of Duplex Doppler in the Diagnosis of Varicocele

Dr. Shpetim Telgrafi, Associate Professor of Urology, reviewed the NYU experience with the use of duplex Doppler in the diagnosis and treatment of varicoceles in male infertility. In men presenting with infertility, there was a 38% incidence of clinical varicoceles; ultrasound diagnosed varicoceles in 76% of the men presenting. As many as 38% of the men were either underdiagnosed

diagnosed exclusively by ultrasound was comparable to the improvement seen in men with clinically diagnosed varicoceles. The use of testicular duplex Doppler with an experienced ultrasonographer is recommended.

Percutaneous Embolization of Varicoceles

Dr. Robert Rosen reviewed the literature on the radiographic embolization of varicoceles. Most centers use stainless steel coils and do embolization under local sedation, so that patients recuperate rapidly. Like surgical repair, embolization offers excellent results in terms of pain control and pregnancy results. Though it is the preferred method of varicocele treatment at some centers, the importance of an experienced

The Future of the Urologist in Managing Infertility

Dr. Arnold Belker reviewed the importance of the urologist in the diagnosis and treatment of infertility. The urologist is, and will be, important in order to:

1. Identify potentially correctable conditions (eg, varicoceles, ejaculatory duct obstruction, iatrogenic obstruction);
2. Identify irreversible conditions, some of which cannot be treated with the male partner's sperm (eg, congenital bilateral absence of the vas deferens, maturation arrest, Klinefelter's syndrome, Sertoli cells only);
3. Identify life-threatening or health-threatening problems (eg, testicular tumors, cystic fibrosis genes);
4. Avoid costly and potentially dangerous advanced reproductive technology; and
5. Be an educator and advocate for the male partner in the harrowing process of infertility. ■